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Brain stimulation over the frontopolar cortex enhances motivation to exert effort for reward

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Abstract: Background: Loss of motivation is a characteristic feature of several psychiatric and neurological disorders. However, the neural mechanisms underlying human motivation are far from being understood. Here, we investigate the role that the frontopolar cortex (FPC) plays in motivating cognitive and physical effort exertion by computing subjective effort equivalents. Methods: We manipulated neural processing with transcranial direct current stimulation targeting the FPC while 141 healthy participants decided whether or not to engage in cognitive or physical effort to obtain rewards. Results: We found that brain stimulation targeting the FPC increased the amount of both types of effort participants were willing to exert for rewards. Conclusions: Our findings provide important insights into the neural mechanisms involved in motivating effortful behavior. Moreover, they suggest that considering the motivation-related activity of the FPC could facilitate the development of treatments for the loss of motivation commonly seen in psychiatric and other neurological disorders.

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Running head: FPC stimulation enhances motivation

Brain stimulation over frontopolar cortex enhances motivation to exert effort for reward

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Abstract

BACKGROUND: Loss of motivation is a characteristic feature of several psychiatric and neurological disorders. However, the neural mechanisms underlying human motivation are far from being understood. Here, we show that frontopolar cortex (FPC) plays a crucial role in motivating cognitive and physical effort exertion by computing subjective effort equivalents.

METHODS: We manipulated neural processing with transcranial direct current stimulation targeting FPC while 141 healthy participants decided whether or not to engage in cognitive or physical effort to obtain rewards.

RESULTS: We found that brain stimulation targeting FPC increased the amount of both types of effort participants were willing to exert for rewards.

CONCLUSIONS: Our findings provide important insights into the neural mechanisms involved in motivating effortful behaviour and suggest that further exploration of FPC function could facilitate the development of treatments for the loss of motivation commonly seen in psychiatric and other neurological disorders.

From sports to academic achievement, motivation determines the levels of energy or other resources a person will invest towards achieving a valued outcome and is thus a core aspect of goal-directed behaviour. Conversely, loss of motivation in goal-directed behaviour is a defining (negative) symptom of several psychiatric and neurological disorders (1-3). Thus, a better understanding of the brain mechanisms involved in motivation and in driving some humans to work harder than others for the same rewards is important for both basic and clinical sciences.

One region that might play a key role in motivation is the frontopolar cortex (FPC). Thought to lie at the top of the hierarchy of a prefrontal control network (4, 5), the FPC is well positioned to support a multipurpose construct such as motivation. Activation in the FPC, as well as in other hubs of the prefrontal control network, correlates with individual measures of motivation and with successful performance in incentivized tasks requiring high cognitive effort (6, 7). However, since this research examined brain activation correlated with successful performance of cognitively demanding tasks, it is unclear whether the observed FPC activity supports cognitive processes required for task performance or whether it plays a more direct role in generating or evaluating motivation itself. If FPC facilitates successful goal-directed behaviour by representing higher-order goals that should be pursued during a given task (6, 7), we expect FPC activity to increase the willingness to engage in effort in order to attain the current task goal. This is also suggested by recent studies showing the FPC to be crucially involved in overcoming various types of costs in order to pursue more valuable goals (8-13). By extension, the FPC involvement in incentivized cognitive tasks (6, 7) might thus be explained by its more general role for boosting the value of goals against the required costs. The first aim of this study was therefore to test the FPC's potential role in motivating effortful goal-directed behaviour in the absence of requirements for high levels of cognitive control or concerns about accurate task performance.

Until now, FPC has been associated primarily with effort related to cognitive control. A second question we addressed was therefore whether and how the FPC may also contribute to motivating physical effort. In other words, is the role of FPC in motivation domain general? Current evidence on this question is mixed, as effort costs in cognitive versus physical tasks have been associated with either common or distinct neural activity in different reports (14-16). Thus, it remains unclear whether overlapping or dissociable neural mechanisms are responsible for motivating the exertion of cognitive and physical effort.

To test the role of FPC in the motivation to exert cognitive or physical effort, we applied transcranial direct current stimulation (tDCS) over right FPC while participants decided whether or not to engage in cognitive or physical tasks that yielded varying levels of reward. tDCS is a non-invasive brain stimulation technique that can be used to either increase or decrease the neural excitability of a brain region (17). This allowed us to examine the impact of tDCS targeting FPC on the willingness to engage in rewarded cognitive and physical effort.

Materials and Methods

Participants

141 healthy humans (mean age = 22.78 years, range 18-34 years, 71 females) participated in the study after they gave voluntary informed consent. Power calculations based on two previous studies administering FPC tDCS in human decision-making tasks (10, 11) suggested a minimum sample size of 42 participants per tDCS group to be required for a 80% probability of finding a significant effect (alpha = 0.05). One participant was excluded because his German language skills were insufficient for understanding the instructions for the cognitive effort task, another participant because the tDCS electrodes slipped during the course of the experiment and a third due to an unusually high number of response omissions (31% of all trials; all other participants: mean omission rate = 0.7%, standard error of mean =

0.1%). Thus, the data of 138 participants were entered into the statistical analyses (anodal tDCS: N = 43, cathodal tDCS: N = 47, sham tDCS: N = 48). The rating task data of one participant were lost due to technical problems, but his choice data from the decision tasks were included in the analyses. Participants received 60 Swiss francs for their participation plus a monetary bonus depending on their choices (see below). The study was approved by the local ethics committee (Cantonal ethics committee Zurich).

Stimuli and task design

In each trial, participants decided whether they were willing to exert a level of cognitive or physical effort to obtain a monetary reward (Figure 1A/B). For physical effort exertion, they had to squeeze a dynamometer for 20 s with 20%-100% of their maximum grip force, whereas for cognitive effort exertion they had to cross all “e” in a text composed of random letter sequence groupings (i.e. pseudo-words) according to a demanding rule (the two letters before and the two letters after an “e” must not comprise vowels). Here, 100% cognitive effort meant that participants had to work on 40 lines of text, a value determined in pilot experiments.

The magnitude of the monetary reward was symbolized by the number of red apples (0, 1, 3, 6, 9, and 12 apples; one apple was exchanged for CHF 0.1 after the experiment.) on a tree, whereas the required effort was indicated at the tree trunk (0%, 20%, 40%, 60%, 80%, and 100% effort). Participants indicated their choices to accept or reject the presented offer via key press during the 3.5 s presentation of an offer. The next offer was presented after an inter-trial interval of 0.5 s (Figure 1C, D).

Note that the goal of the study was to test the FPC’s role in deciding whether or not a reward is worth the effort required to obtain it, not in the actual production of effort after the decision to engage in it. To avoid exhaustion, which might affect cost-benefit computations during decision-making, participants did not have to exert the effort immediately after having accepted an offer. Instead, we randomly selected one trial from both effort decision tasks at the end of the experiment and implemented the chosen decision (Figure 1E). If participants had accepted the chosen offer, they had to exert the corresponding amount of cognitive or physical effort to obtain the additional monetary reward. If they had rejected the offer, they received no additional reward after the experiment. Accordingly, we instructed participants to make each decision during the tasks as if it would be the one randomly selected at the end, because each decision had an equal chance of being selected at the end. We note that such decisions (i.e., whether one is willing to initiate a given amount of effort for a given reward) are impaired in apathy (18, 19). Participants performed 3 blocks each of the cognitive and the physical effort decision tasks, with each block containing 36 trials such that all combinations of reward magnitudes and effort levels were presented once within a block.

In addition to the decision tasks, participants provided two separate ratings during tDCS in which they indicated how much cognitive or physical effort they were willing to invest for the different reward levels as well as the subjective strain of the effort levels used in the experiment. However, these data are not discussed in the current manuscript.

tDCS protocol

We applied anodal, cathodal, or sham tDCS using a 16-channel tDCS stimulator (neuroConn, Ilmenau, Germany) over the right FPC region (MNI coordinates: x=32, y=54, z=21) which had been shown to correlate with individual differences in the successful exertion of rewarded cognitive effort (6). It should be noted, however, that this study had found motivation-related activation in the left FPC as well (although weaker than for right FPC). We therefore do not intend to make any claims about lateralization in the current study. In 28 participants, we used T1-scans of each participant to determine the centre point of the electrode over the FPC. As we found the centre of the active electrode to be reliably placed 1 cm ventrally to electrode position R2 on a Waveguard Duke 128 channels cap in these participants, we fixed the electrode at this electrode position for the remaining participants. A second electrode was placed over the vertex (electrode position Z7 on the 128-channel cap). As FPC and vertex electrodes, we applied standard 5x5 and 10x10 cm electrodes, respectively, fixed by rubber straps. We used larger reference than active electrodes to minimize the stimulation effect at the vertex relative to the FPC site (20). Figure S1 illustrates electrode positioning and the modeled current density for anodal stimulation (21).

During task performance, we stimulated with 1.5 mA current strength in the active anodal and cathodal groups, while in the sham group the current was turned off after 30 s. To account for possible delays in the onset of tDCS effects, participants had to wait 4 minutes following stimulation onset before they started the decision tasks. Stimulation was turned off when participants had finished all experimental tasks (mean stimulation duration = 23 min, range = 21-27 min).

Data analysis.

We analysed behavioural responses in the decision tasks with mixed-effects generalized linear models (MGLMs) as implemented in IBM SPSS 22 (see *SI Methods* for the equations and detailed explanations relating to each model). In all MGLMs, effects of tDCS were modelled predictors for anodal tDCS (1 for anodal tDCS group and 0 for sham and cathodal groups) and cathodal tDCS (1 for cathodal group and 0 for anodal and sham groups) that allow assessing the effects of anodal and cathodal tDCS relative to the sham group (*SI Methods*). Parameters were estimated using maximum-likelihood methods. The alpha threshold was set to 5%.

Results

Baseline measures and task validation

The three tDCS groups were well balanced with respect to baseline apathy (Lille apathy rating scale (19)), reward sensitivity (behavioural inhibition/activation system (22)), and anhedonia (Snaith-Hamilton pleasure scale (23)), Kruskal-Wallis test, all $\chi^2 < 4.20$, all $p > 0.12$ (*SI Methods* and Table S1). In addition, to control for potential tDCS effects on emotional state, we measured participants' mood, alertness, and calmness before the start and at the end of stimulation using a multidimensional mood state questionnaire (24). FPC-targeted tDCS did not change participants' emotional state over the course of the experiment, all $\chi^2 < 1.89$, all $p > 0.39$ (Table S2). Thus, it is unlikely that potential tDCS effects on choices are confounded by baseline group differences in motivation or emotional state.

Lastly, the correlations between the action initiation scale of the Lille apathy rating scale (a measure of apathy (19, 25)) and mean accepted offers to exert both cognitive effort, r = 0.24, p = 0.05, and physical effort, r = 0.26, p = 0.04, suggest that the current choice task is weakly related to a subset of the factors contributing to clinical apathy (see also discussion section)..

Anodal tDCS over FPC increases willingness to engage in cognitive and physical effort

To test whether FPC-targeted tDCS modulates the motivation to engage in cognitive and physical effort, we computed an MGLM (MGLM-1) in which we regressed the mean probability of accepting an offer on predictors for anodal tDCS, cathodal tDCS, Effort type (cognitive vs. physical), Effort level (0%, 20%, 40%, 60%, 80%, or 100%), Reward magnitude (0, 1, 3, 6, 9, or 12 apples), as well as the interactions between Effort type, Effort level, Reward magnitude, and anodal or cathodal tDCS. Participants were more willing to engage in effort under anodal (46%) than under sham tDCS (38%), $\beta = 0.109$, $t(6769) = 3.66$, $p < 0.001$, whereas cathodal tDCS (39%) showed no significant effect compared to sham, $\beta = 0.021$, $t(7436) = 0.73$, $p = 0.47$. The effect size for the mean difference between anodal and sham tDCS (which was computed based on the means and standard deviations for acceptance rates in these groups) was small to moderate (Cohen's d = 0.46). This result is consistent with our hypothesis and suggests that FPC-targeted anodal tDCS improved the motivation to engage in rewarded effort (Figure 2).

The effects of the Effort Level and Reward Magnitude regressors estimated in MGLM-1 indicate that participants used both of these decision-relevant variables in making their choices. Specifically, we found a negative effect of Effort level, $\beta = -0.330$, $t(712) = 9.54$, $p < 0.001$, a positive effect of Reward magnitude, $\beta = 0.072$, $t(672) = 22.42$, $p < 0.001$, and an Effort level × Reward magnitude interaction, $\beta = -0.044$, $t(466) = 7.66$, $p < 0.001$. In our regression specification (see SI Methods) these coefficients quantify the behavioural patterns of the sham stimulation group and indicate that, as expected, the positive effect of reward magnitude on choosing to engage in effort decreased with increasing effort levels required to obtain the reward (Figure 3-4, Table S3). Anodal tDCS significantly reduced the discounting of reward by effort level as indicated by a 3-way interaction between Anodal tDCS, Effort level, and Reward magnitude, $\beta = 0.027$, $t(6049) = 3.65$, $p < 0.001$ (Figure 3D/4D). There was no significant 3-way cathodal tDCS × Effort level × Reward magnitude interaction, $\beta = 0.012$, $t(6855) = 1.71$, $p = 0.09$ (Figure 3E/4E). However, cathodal tDCS did increase the impact of Effort level on choices, $\beta = -0.103$, $t(4295) = 2.18$, $p = 0.03$, indicating that the demotivating effects of effort were stronger under cathodal than sham tDCS even though this reduced motivation did not result in a significant reduction in accepted offers overall.

It is important to note that the tDCS effects on motivation were independent of the specific type (i.e., cognitive or physical) of effort. Although participants accepted more offers that required physical versus cognitive effort, $\beta = 0.063$, $t(9502) = 2.40$, $p = 0.02$, and the demotivating effect of Effort level was stronger for physical than cognitive effort, $\beta = -0.091$,

$t(9502) = 2.10$, $p = 0.04$, there was no evidence that stimulation effects differed between the cognitive and physical effort tasks, all $t < 1.76$, all $p > 0.08$ (Table S3).

To assess the specificity of stimulation effects in more detail, we computed two further MGLMs. These MGLMs separated trials requiring cognitive (MGLM-1C) and physical effort (MGLM-1P) into different regression models, but otherwise included the same predictors as MGLM-1. These MGLMs yielded the same pattern of results as MGLM-1 for anodal stimulation (Tables S4-5). For both cognitive and physical effort, anodal stimulation enhanced the propensity to engage in rewarded effort by reduced the discounting of rewards at higher effort levels, anodal tDCS × Effort level × Reward magnitude: both $\beta > 0.024$, both $t > 3.22$, both $p < 0.001$. FPC-targeted anodal tDCS thus increased the willingness to exert both cognitive and physical effort. When splitting the trials by effort type, cathodal stimulation was found to significantly reduce motivation as function of effort level for cognitive effort, $\beta = -0.102$, $t(1203) = 2.21$, $p = 0.03$, but not physical effort, $\beta = -0.001$, $t(1696) = 0.01$, $p = 0.99$ (Tables S4-5). However, we must exercise caution in drawing conclusions about potential differences between the effects of cathodal tDCS over FPC on cognitive and physical effort given the lack of significant interaction effects in the full version of MGLM-1, which included all trials in the same model.

Discussion

We examined the impact of brain stimulation targeting FPC on motivating the exertion of cognitive or physical effort for rewards. Our results demonstrate that FPC-targeted anodal tDCS, relative to sham and cathodal tDCS, increased participants' willingness to exert rewarded cognitive and physical effort, providing a causal link between brain processes and the motivation to engage in effortful goal-directed behaviour. In particular, anodal stimulation counteracted the devaluation of rewards by higher effort levels, which suggests that stimulation modulated the trade-off between required effort costs and the associated rewards rather than participants' sensitivity to potential gains or effort costs in isolation.

The similar stimulation effects on cognitive and physical effort indicate that FPC is a domain-general facilitator of motivation in effort-based decision-making. Thus, our findings corroborate previous neuroimaging studies involving FPC in motivating cognitive control (6, 7). However, our results also indicate a broader role for FPC in computing whether the reward at stake is worth the required effort independently of whether the required demands are cognitive or physical.

The precise function of FPC in decision making is still a matter of active investigation and debate (25). One frequently proposed FPC function is to evaluate the reward value of an overarching goal (5, 7) and promote exploratory actions that are costly in the short-term but beneficial in the long-run (9, 10, 12). Recent studies have shown that FPC also influences the implementation of precommitment strategies that restrict one's own action space (i.e. represent a cost in terms of freedom to choose) to ensure one will obtain the most favourable outcome (8, 11). Combining these previous findings with our results, we suggest that FPC plays an important role in determining whether or not a potential reward is worth the cost (i.e., monetary payoff, freedom, or effort) required to obtain it.

Our results further indicate the need to extend current neural systems models of effort-based decision-making. Previous studies have associated cost-benefit weighting with anterior cingulate cortex (ACC) and the dopaminergic nigrostriatal system (14, 16, 18, 26-29), while subjective strain of cognitive and physical effort correlated with activity in lateral prefrontal cortex and supplementary motor cortex, respectively (13, 14, 18, 30). Specifically, ACC and the striatum are thought to integrate reward and effort signals such that the required effort diminishes the value of potential rewards. While previous studies on effort-based decision-making did not consider a potential role of FPC, our results suggest that the FPC causally contributes to motivating effortful goal-directed behaviour. It is likely that the FPC functions in concert with nigrostriatal networks, the ACC, and/or other brain regions involved in cost-benefit weighting.

Please note that the observed stimulation effects cannot be explained by a change in risk preferences, because the probability of success was virtually one in the executed effort tasks (all participants successfully completed the practice tasks for cognitive and physical effort prior to stimulation). It is further unlikely that tDCS modulated time preferences, because tDCS similarly affected decisions in the cognitive and physical effort task, even though the performance of the text editing task for cognitive effort took considerably longer (up to 10 min) than physical effort exertion (squeezing the handgrip for 20 s).

Before concluding, we note three limitations of the current work. The first concerns the relatively low spatial resolution of tDCS (31). However, the finding that FPC-targeted tDCS improves motivation is consistent with neuroimaging results showing correlations between FPC activation and the likelihood to engage in rewarded effort (6). In addition, a current density model suggests that tDCS effects were most pronounced in FPC rather than in other regions (Figure S1), even though we cannot entirely exclude that tDCS also affected other brain regions that may be related to anhedonia, e.g. subgenual ACC (29), or to value processing, e.g. ventromedial prefrontal cortex (32). However, we have recently shown that FPC-targeted tDCS affects specifically meta-cognitive processes rather than other processes associated with adjacent brain regions, such as reward processing or self-control (10, 11). Together these findings indicate that changes in excitability of FPC are the most likely cause for the observed tDCS effects. A second limitation, the weaker effects of cathodal relative to anodal tDCS, is consistent with a meta-analysis showing that anodal tDCS may have more robust effects on cognition than cathodal tDCS (33). In any case, the opposite, motivation-reducing impact of cathodal tDCS suggests that the motivation enhancement by anodal tDCS was not due to unspecific stimulation effects (like increased arousal or discomfort) present in prolonged real but not sham stimulation. Third, due to the small to moderate size of the stimulation effect, it would be useful to continue this line of research in order to determine which patient groups benefit most from the stimulation and which might be better served by other treatments. Lastly, it is important to note that we studied decisions to exert effort separately from the actual production of the effort, which differs from the approach commonly taken in studies relating clinical symptoms such as apathy to laboratory effort tasks (1). In previous work, effort had to be exerted immediately after each decision to engage in it (but see (16, 34)). While from a methodological perspective our current approach allows us to isolate the process of deciding whether or not to engage in effort, from a clinical perspective "apathy" is a multi-facet construct that entails both the original decision to engage and subsequent decisions to continue exerting effort ("avolition") as well as other factors such as emotional sensitivity ("anhedonia") and social motivation ("asociality") (35, 36). It is known that apathy is strongly related to fatigue, the subjective feeling of exhaustion due to effort exertion, which may affect an individual's willingness to engage in effort (37). As noted above, we designed our experiment to exclude (changes in) fatigue as a driving factor in decisions to engage in effort. However, as a consequence our data cannot be used to determine how stimulation over FPC interacts with fatigue or the learning from either effort or reward feedback. Given empirical evidence for the independence of the distinct apathy subcomponents (1, 35, 36), it is important to emphasize that the experimental procedure we applied specifically measures the general willingness to initially engage in effort, rather than apathy as global construct.

The current results are relevant for psychiatric disorders characterized by a loss of motivation (1-3) and speak to a motivation-based separation of healthy aging from cognitive decline and dementia (38, 39). For example, in patients with schizophrenia, apathy correlates negatively with the willingness to exert physical effort (1-3) and effort discounting in apathy is most pronounced when high levels of effort are required (19). Strikingly, in the current study, tDCS not only increased willingness to exert effort but also counteracted the devaluation of reward at particularly high effort levels. Lastly, previous work has shown that FPC thickness is reduced in patient groups suffering from anhedonia relative to healthy controls (40-42) and strokes affecting the FPC lead to apathy (43). In conjunction with these results, our findings highlight the potential of enhancing FPC function as an alternative or complimentary treatment strategy for apathy-related disorders.

Supplementary Materials

SI Methods

SI Results

Figure S1

Tables S1-S6

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Data availability

The data that support the findings of this study are available on https://osf.io/bh6ft/.

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Figures

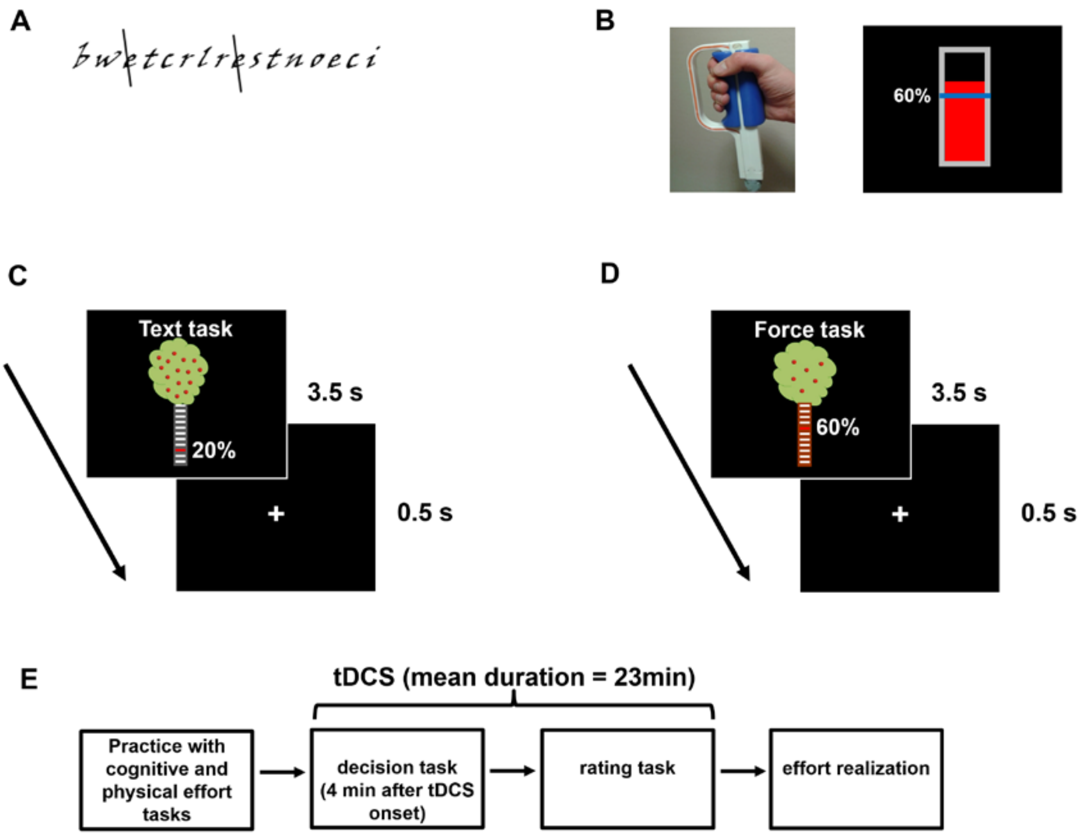

Figure 1. Effort types, task design, and task validation. (A) Cognitive effort consisted of letter identification in a demanding text task (crossing letters “e” unless one of the two letters before or after comprised a vowel) and effort levels varied as a function of text length. (B) Physical effort consisted of squeezing an isometric handgrip dynamometer and effort levels varied as a function of the force required (60% maximum strength in the displayed example). (C, D) Example decision trial of decision task. In each trial, participants decided whether to accept or reject offered combinations of (C) cognitive or (D) physical effort and monetary reward. The magnitude of the reward at stake was illustrated by the number of apples on the tree, the required effort was indicated by the trunk height. Effort type was indicated above the tree (“text task” for cognitive effort, “force task” for physical effort). Participants had to decide during the presentation of the tree for 3.5 s. (E) Overview over experimental procedure.

Participants first exerted examples of cognitive and physical effort. Thereby they experienced the meaning of different effort levels of the two effort types used in subsequent tasks. Next, participants performed the decision task and the rating tasks while receiving anodal, sham, or cathodal tDCS. At the end of the experiment, one choice of the decision task was randomly selected and participants had to exert the selected amount of cognitive or physical effort.

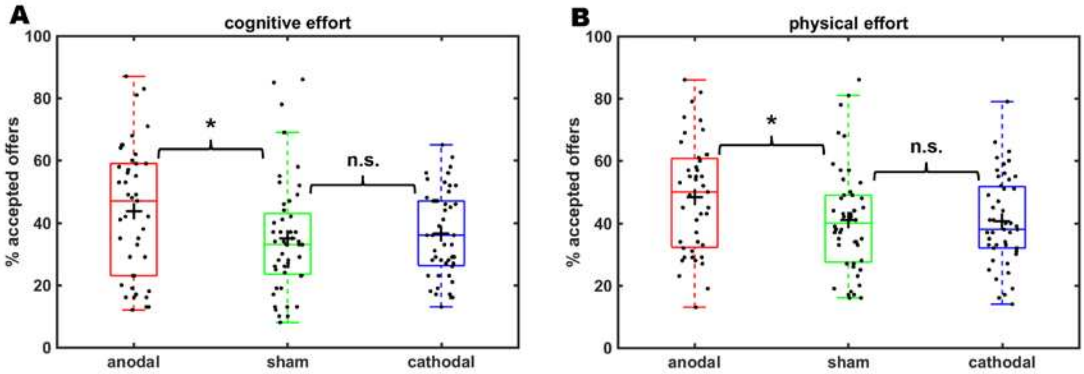

Figure 2. Boxplots illustrating the main effects of anodal and cathodal tDCS on decision behaviour. The percentages of decisions to exert cognitive or physical effort are shown separately for anodal, sham, and cathodal tDCS. Coloured boxes indicate median and interquartile range. Black dots illustrate choices of individual participants, means are indicated by black crosses (+). Anodal tDCS, relative to sham and cathodal tDCS, significantly increased participants' motivation to exert cognitive or physical effort for a reward. Asterisks (*) indicate significant results ($p < 0.05$).

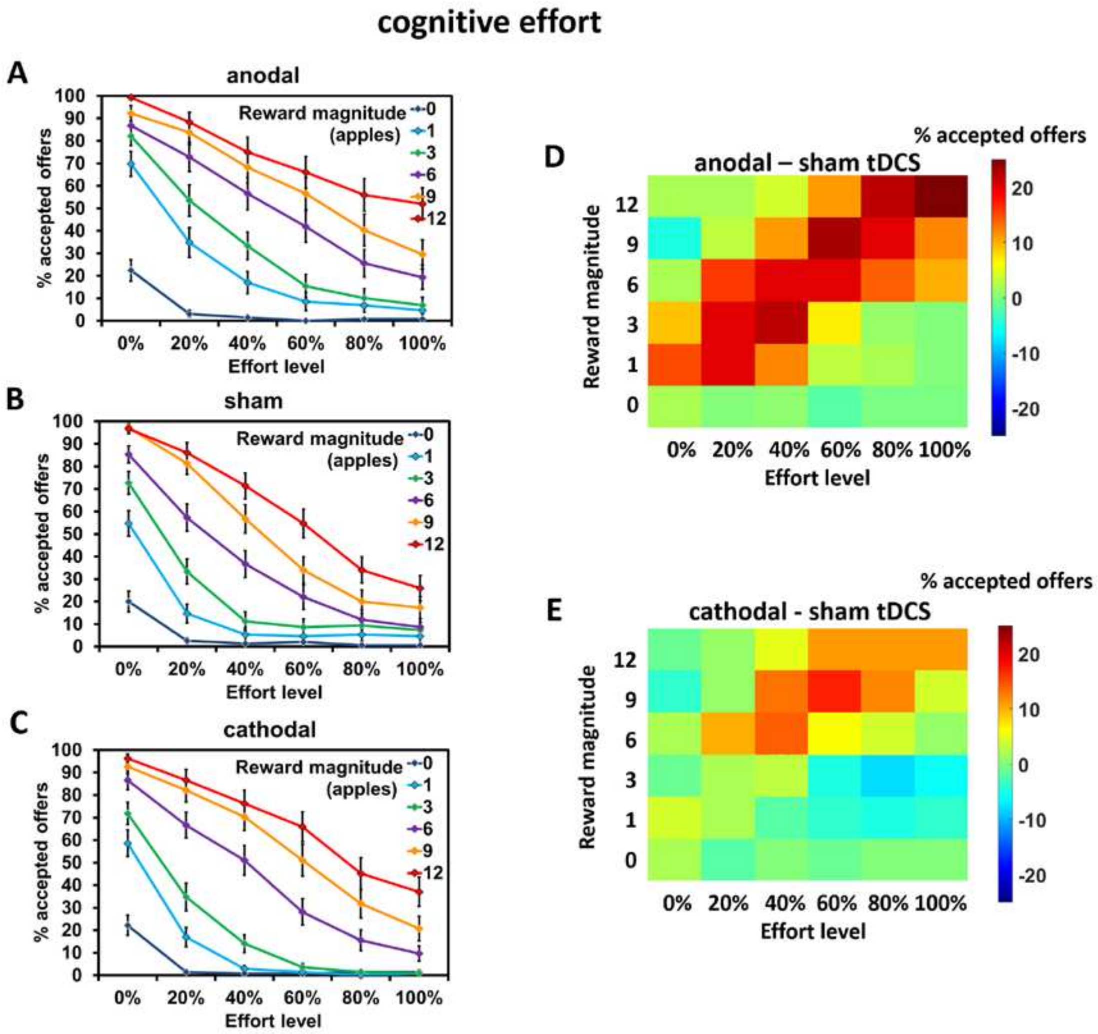

Figure 3. Illustration of the effects of stimulation on willingness to exert *cognitive effort* as a function of effort level and reward magnitude, separately for (A) anodal, (B) sham, and (C) cathodal tDCS. Error bars indicate standard error of the mean. (D, E) shows heatmaps illustrating the effects of stimulation (anodal – sham tDCS and cathodal – sham tDCS) on willingness to accept offers in the cognitive effort task as a function of effort level and reward magnitude. The colour scale indicates the tDCS-induced change in acceptance rates in percentage as a function of each effort level and reward magnitude combination. The three-way interactions between anodal tDCS, Reward magnitude, and Effort level can be seen from the shift in warmer colours (i.e. higher acceptance rates) toward the upper right corner of plot (D)

showing the difference between anodal and sham tDCS groups. This suggests that anodal tDCS (relative to sham tDCS) reduced the discounting of rewards with increasing effort levels.

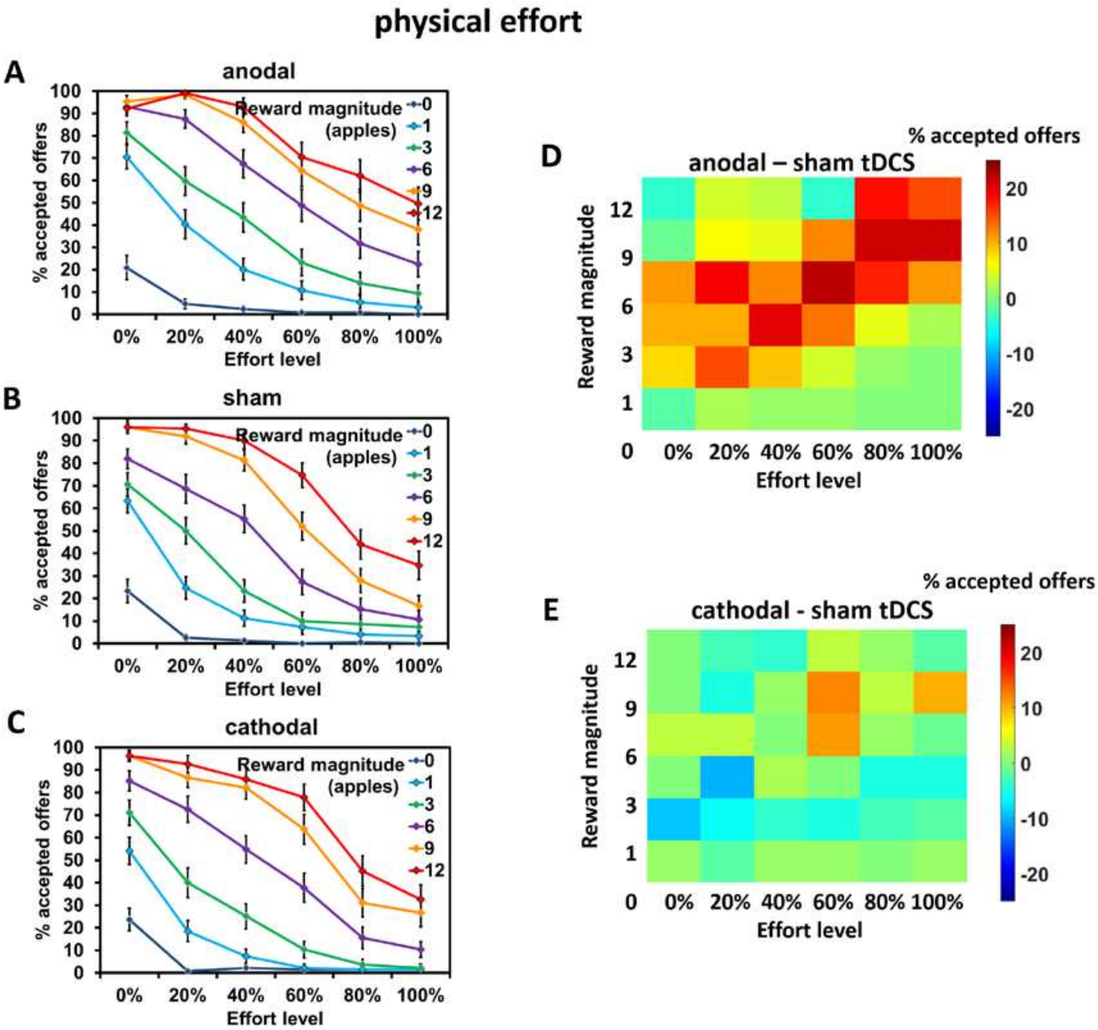

Figure 4. Illustration of the effects of stimulation on willingness to exert *physical effort* as a function of effort level and reward magnitude, separately for (A) anodal, (B) sham, and (C) cathodal tDCS. Error bars indicate standard error of the mean. (D, E) shows heatmaps illustrating the effects of stimulation (anodal – sham tDCS and cathodal – sham tDCS) on willingness to accept offers in the physical effort task as a function of effort level and reward magnitude. The colour scale indicates the tDCS-induced change in acceptance rates in percentage as a function of each effort level and reward magnitude combination. As for the cognitive effort task, the shift in warmer colours (i.e. higher acceptance rates) toward the upper right corner of plot (D) showing the difference between anodal and sham tDCS groups

suggests that anodal tDCS (relative to sham tDCS) reduced the discounting of rewards with increasing effort levels.